UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,453	04/16/2001	Dan M. Granoff	CHIR-0283	1041

7590 10/26/2007

Alisa A Harbin
Chiron Corporation
Intellectual Property R338
PO Box 8097
Emeryville, CA 94662

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
10/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/701,453	GRANOFF ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-22 and 24-30* is/are pending in the application.

4a) Of the above claim(s) *29* is/are withdrawn from consideration.

5)☒ Claim(s) *26-28 and 30* is/are allowed.

6)☒ Claim(s) *17-19, 21, 22, 24 and 25* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 10/01/07, 06/15/07 and 07/24/07 in response to the non-final Office Action mailed 01/22/07. The former is compliant with 37 CFR 1.121.

Status of Claims

2) Claim 23 has been canceled via the amendment filed 10/01/07.

Claim 17 has been amended via the amendment filed 10/01/07.

New claim 30 has been added via the amendment filed 10/01/07.

Claims 17-22 and 24-30 are pending.

Claims 17-22, 24-28 and 30 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claim 23 made in paragraph 11 of the Office Action mailed 01/22/07 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992 - already of record) in view of Seid Jr. *et al.* (US 7,118,757) ('757), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

6) The rejection of claims 17-19, 21, 22 and 25 made in paragraph 11 of the Office Action mailed 01/22/07 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) in view of Seid Jr. *et al.* (US 7,118,757, already of record) ('757),

is withdrawn in light of Applicants' amendment to the base claim.

7) The rejection of claim 24 made in paragraph 12 of the Office Action mailed 01/22/07 under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) as modified by Seid Jr. *et al.* (US 7,118,757, already of record) ('757) as applied to claim 17 above, and further in view of Seid (US 6,638,513, already of record) ('513), is withdrawn in light of Applicants' amendment to the base claim.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C § 103

8) Claims 17-19, 21, 22 and 25 are rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) in view of Seid Jr. *et al.* (US 7,118,757, already of record) ('757) and O'Hagan (*J. Pharm. Pharmaco.* 50: 1-10, January 1998).

The reference of Seid Jr. *et al.* ('757) is applied in this rejection because it qualifies as prior art under subsection (e) of 35 U.S.C § 102 and accordingly is not disqualified under U.S.C 103(a).

Costantino *et al.* taught a conjugate vaccine comprising immunologically effective amounts of group C meningococcal oligosaccharides conjugated to CRM 197 and aluminium hydroxide, and a method of inducing an immune response to group C *Neisseria meningitidis* by administering an immunologically effective amount of the vaccine to a subject (see page 693).

Costantino *et al.* do not teach the use in their conjugate vaccine of MF59 adjuvant and outer membrane vesicles from a strain of group B *Neisseria meningitidis*, including the strain 44/76 of group B *Neisseria meningitidis*.

However, Seid Jr. *et al.* ('757) disclosed a vaccine formulation (i.e., immunogenic composition) comprising appropriate concentration of isolated outer membrane vesicles (OMVs) from *Neisseria meningitidis*, including serogroup B *Neisseria meningitidis* strain H44/76 (B:15:P1,7.16), and expressly taught that these OMVs can be used in mixtures, multivalent vaccines, or in conjunction with other antigens of *Neisseria meningitidis,* including oligosaccharide or polysaccharide capsular components of serogroup C *Neisseria meningitidis* with or without conjugation to a protein such as non-toxic mutant CRM197 using standard techniques for coupling saccharides to proteins. Seid Jr. *et al.* ('757) taught that their meningococcal OMV vaccine formulation contains an adjuvant and can advantageously contain preferably meningococcal C

capsular polysaccharides covalently coupled to a protein carrier such as a nontoxic CRM mutant, a *Salmonella* flagellin, or a human albumin. See 'Summary of the Invention' in column 2; paragraph bridging columns 3 and 4; Example 1B; first and second full paragraphs in column 10; lines 38-45 in column 4; paragraph bridging columns 10 and 11; Examples 14 and 15; and Table 5B depicting MenC-CRM197 conjugate plus alum. Encompassed within the scope of Seid Jr.'s ('757) meningococcal C capsular polysaccharides and Seid Jr.'s protein carrier respectively are depolymerized meningococcal C capsular polysaccharides, i.e., oligosaccharides (see Examples 10 and 14), and CRM197. See the sentence bridging columns 9 and 10; and Table 5B depicting MenC-CRM197 conjugate plus alum. Via Examples 10 and 14, Seid Jr. *et al.* ('757) taught how to conjugate a serogroup C meningococcal depolymerized capsular polysaccharide (i.e., oligosaccharide) to one of the above-mentioned protein carriers. Seid Jr. *et al.* ('757) further taught that the polysaccharide (meaning meningococcal polysaccharide) vaccine can be enhanced by a vaccine according to their invention as a vaccine with broad, extensive action against most serotypes. Seid Jr. *et al.* ('757) taught that since meningococcal disease is currently caused chiefly by group B meningococci and because the class 1 outer membrane proteins (present in the OMV formulations) occurring in group B meningococci also occur in group A, C, W-135 and Y meningococci, the vaccines of their invention should be effective in preventing disease caused by group A, C, W-135 and Y. See first full paragraph in column 4.

MF59 was known in the art to be a more potent and safe adjuvant compared to alum in human subjects for use with several vaccines. For instance, O'Hagan taught MF59-containing adjuvant to be significantly more potent than alum, inducing 5-50-fold higher antibody titers in a number of animals compared to alum. See abstract and paragraph bridging pages 5 and 6 of O'Hagan. From all clinical trials, it was concluded that M59 adjuvant is safe and effective in man in combination with a variety of antigens. Most importantly, O'Hagan taught that the range of antigens for which MF59 is effective was extended to include a polysaccharide-protein conjugate vaccine such as a Group C meningococcal oligosaccharide-CRM197 by Granoff *et al. Infect. Immun.* 65: 1710-1715, 1997. See left column on page 6 of O'Hagan and the reference of Granoff *et al.* cited at the end of left column on page 9.

Given the express teaching of Seid Jr. *et al.* ('757) that meningococcal OMV formulations can be used in conjunction with other antigens of *Neisseria meningitidis* including oligosaccharide

or polysaccharide capsular components of serogroup C *Neisseria meningitidis* conjugated to a protein carrier such as non-toxic mutant CRM197 and the express teaching of O'Hagan that MF59-containing adjuvant is significantly more potent than alum inducing 5-50-fold higher antibody titers in a number of animals compared to alum, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace alum in Costantino's group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate vaccine with O'Hagan's MF59 and then combine with Seid Jr.'s ('757) outer membrane vesicle vaccine formulation made from the group B meningococcal reference strain H44/76 to produce the instant invention, with a reasonable expectation of success. Given the express teaching of Seid Jr. *et al.* ('757) that the class 1 outer membrane proteins present in their group B meningococcal OMV formulations also occur in other groups including groups A, W-135 and Y meningococci and the express teaching by O'Hagan that the use of the safe and more potent MF59 can be extended Group C meningococcal oligosaccharide-CRM197 conjugate vaccine, one of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing a mixed or multivalent vaccine that uses Seid Jr.'s ('757) H44/76 B *Neisseria meningitidis* outer membrane vesicles (OMVs) advantageously in conjunction with a group C *Neisseria meningitidis* oligosaccharide-CRM_{197} conjugate and provides broad, extensive action against most serotypes and is effective in preventing disease caused by group A, C, W-135 and Y as taught by Seid Jr. *et al.* ('757) and a vaccine that contains an adjuvant that is proved in the art to be safe and more potent than alum as taught by O'Hagan.

Claim 22 is a product-by-process claim which includes the process limitation: 'vesicles are produced by a deoxycholate extraction process'. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the

prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art group B meningococcal outer membrane vesicles differs from that of the instantly claimed vesicles.

Claims 17-19, 21, 22 and 25 are *prima facie* obvious over the prior art of record.

9) Claim 24 is rejected under 35 U.S.C § 103(a) as being unpatentable over Costantino *et al.* (*Vaccine* 10: 691-698, 1992, already of record) as modified by Seid Jr. *et al.* (US 7,118,757, already of record) ('757) and O'Hagan (*J. Pharm. Pharmaco.* 50: 1-10, January 1998) as applied to claim 17 above, and further in view of Seid (US 6,638,513, already of record) ('513).

The reference of Seid ('513) is used in this rejection because it qualifies as prior art under 35 U.S.C § 102(e) and therefore is not disqualified as prior art under 35 U.S.C § 103(a).

The teachings of Costantino *et al.* as modified by Seid Jr. *et al.* ('757) and O'Hagan are explained above, which do not teach their composition to be further comprising polylactic acids or polyglycolic acids.

However, the use of polylactic acids or polyglycolic acids in combination with a meningococcal oligosaccharide conjugate was well known in the art at the time of the instant invention. For instance, Seid ('513) taught combining carriers, such as, polylactic or polyglycolic acids with meningococcal glycoconjugates for the purpose of primary vaccination wherein carriers do not themselves induce the production of harmful antibodies (see lines 10-18 in column 9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to add Seid's ('513) polylactic or polyglycolic acid to Costantino's immunogenic composition as modified by Seid Jr. *et al.* ('757) and O'Hagan to produce the instant invention, with a reasonable expectation of success. One of ordinary skill in the art would have been motivated to produce the instant invention for the expected benefit of providing Costantino's immunogenic composition as modified by Seid Jr. *et al.* ('757) and O'Hagan for primary vaccination without inducing the production of harmful antibodies as taught by Seid ('513).

Claim 24 is *prima facie* obvious over the prior art of record.

Remarks

10) Claims 17-19, 21, 22, 24 and 25 stand rejected. Claims 20 stands objected to as being dependent from a rejected claim. Claims 26-28 and 30 are allowable.

11) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office

action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

13) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

14) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Acting supervisor, Bruce Campell, can be reached on (571) 272-0974.

S. DEVI, PH.D.
PRIMARY EXAMINER

October, 2007